claims 41-42 and 57, the product claims, be examined along with the elected invention under MPEP §806.05(i) as Examiner previously stated in Office Action Paper No. 5.

35 U.S.C. §112 second paragraph

The Examiner rejected claims 43 and 52-55 under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the interest of expediting prosecution, the Applicant has amended claim 43 for clarity. Applicant respectfully contends that amended claim 43 and dependent claims 52-55 are not indefinite.

The Examiner rejected claim 55 under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Applicant respectfully disagrees with the Examiner that claim 55 is unclear. Claim 55 claims a reformulated oral composition that contains less than all the components of the existing pharmaceutical composition plus the gallic acid ester. This claim, therefore, would cover compositions in which one or more of the components present in the existing pharmaceutical composition is absent in a reformulation of the existing composition. Such a claim encompasses a clearly defined set of possible combinations and is not indefinite.

35 U.S.C. §102 (b)

Cheng *et al.* (EP 819433 A2)

The Examiner rejected claims 23, 32-36, 38-40, 43 and 52-55 under 35 U.S.C. §102(b) as being anticipated by Cheng *et al.* To anticipate a claim, a prior art reference must teach every element of the claim. *See* MPEP § 2131. Independent claim 23 reads as follows:

23. (Amended) A method of formulating an oral pharmaceutical composition, the method comprising:

admixing a pharmaceutical compound, a pharmaceutical carrier, and a gallic acid ester, the gallic acid ester being present in sufficient amount to provide bioavailability of the pharmaceutical compound in the presence of the gallic acid ester greater than the bioavailability of the pharmaceutical compound in the absence of the gallic acid ester when the pharmaceutical

composition is administered orally to a mammal, wherein said gallic acid ester is selected from the group consisting of (-)-epicatechin gallate, (-)-epigallocatechin gallate, (-)-gallocatechin gallate, and tannic acid.

As exemplified in claim 23, the claims at issue contain limitations not found in Cheng.

First, claims of the present invention are directed toward formulation of pharmaceutical compositions that are administered **orally**. Conversely, the cancer drugs of Cheng are limited to cancer drugs that are administered intraperitoneally. Cheng only teaches intraperitoneal administration of the cancer drug (Cheng, page 3, line 41; pages 4-5, Examples 1-4; and page 6, claims 8-10) while allowing for either intraperitoneal administration or oral administration of the antioxidant (Cheng, page 3, lines 42-43; pages 4-5, Examples 1-4; and page 6, claims 8-10). The present invention relates to the oral administration of both the pharmaceutical compound and the gallic acid ester thereby increasing bioavailability of the pharmaceutical compound in the gut. As such, Cheng does not anticipate the present claims.

Second, claims of the present invention are directed toward increasing the bioavailability of the pharmaceutical compound present in the oral pharmaceutical composition. Cheng teaches methods of increasing the efficacy of cancer drugs by administering an antioxidant at the same time as administration of the cancer drug. Cheng does not disclose the use of gallic acid esters to provide increased bioavailability of a pharmaceutical compound. Antioxidant activity does not correlate with enzyme inhibitory activity leading to increased bioavailability. Notably, an antioxidant is "[a] substance which prevents the reaction of various food constituents with oxygen." (Ensminger, A.H. et al., Foods and Nutrition Encyclopedia, 2nd ed., 1:100 (1994), attached) or "substances used to preserve food by retarding deterioration, rancidity or discoloration due to oxidation" (21 C.F.R. 170.3(o)(3), 4-1-98 edition, attached). Antioxidants in foods and drugs act as oxygen and free radical scavengers to prevent chemical and free radical reactions that lead to decomposition of food and drug products. The oxygen and radical scavenging effect of gallic acid esters and other antioxidants is a chemical reaction which is not dependent on the presence of an enzyme (see Stuckey, B.N., "Antioxidants as Food Stabilizers" CRC Handbook of Food Additives, 2nd ed., pp. 185-196 (1980), attached). This is very different from inhibition of drug metabolism where the inhibitor interacts with a particular enzyme to prevent access to an active site or to alter the enzyme configuration. The prior art

does not teach the utility of gallic acid esters for a physiological effect as taught by the present application. As such, Cheng does not anticipate the present claims.

Salatinjants (US 4716173)

The Examiner rejected claims 23, 32-36, 38-40, 43 and 52-55 under 35 U.S.C. §102(b) as being anticipated by Salatinjants. Salatinjants discloses and claims the use of a gallic acid ester, tannic acid, in conjunction with several other compounds to prolong the **residence time** of drugs in the plasma of mammals. The present invention involves increasing the **bioavailability** of a drug as being the fraction of the oral dose that reaches the circulation in an active, unchanged form. Specification, page 1, lines 24-25. Furthermore, Salatinjants refers only to the residence time of the drug in plasma. The present invention refers to increasing the systemic concentration of the drug over time where systemic drug concentration refers to the concentration of drug present in the bodily fluids, such as serum, plasma or blood and the tissues bathed by the systemic fluids, including the skin. Specification, page 3, lines 23-29; page 7, lines 10-16. Additionally, Salatinjants discloses increasing the residence time of only a limited class of drugs – the sulfa and cinchona alkaloid drugs. The present application is not so limited. Specification, page 8, lines 6-14. A reference that merely discloses increasing the residence time of a limited class of drugs cannot anticipate the present claims.

Additionally, the present claims are directed toward a method of formulating an oral pharmaceutical compound, or reformulating an existing pharmaceutical compound, with a gallic acid ester in order to increase bioavailability of the active compound present in the pharmaceutical compound. Salatinjants does not anticipate such claims.

New claims 58 and 59 do not recite the use of tannic acid and are not anticipated by Salatinjants.

As discussed above, the present invention is not anticipated by the prior art. As such, Applicant respectfully contends that the Examiner's rejection regarding inherent properties of the invention has been addressed.

The Commissioner is hereby authorized to charge any fees associated with this communication to Deposit Account No. 03-3117.

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VERSIONS WITH MARKINGS TO SHOW CHANGES MADE

43. (Twice Amended) A method of reformulating [increasing bioavailability of the active compound of] an existing oral pharmaceutical composition, the method comprising:

[reformulating the existing composition to provide a reformulated oral composition by] admixing the active compound of the existing oral pharmaceutical composition with a gallic acid ester, the gallic acid ester being present in sufficient amount to provide bioavailability of the active compound when administered in the reformulated composition greater than said bioavailability of the active compound when administered in the existing pharmaceutical composition, wherein said gallic acid ester is selected from the group consisting of (-)-epicatechin gallate, (-)-epigallocatechin gallate, (-)-gallocatechin gallate, and tannic acid.

58. A method of formulating an oral pharmaceutical composition, the method comprising:

admixing a pharmaceutical compound, a pharmaceutical carrier, and a gallic acid ester, the gallic acid ester being present in sufficient amount to provide bioavailability of the pharmaceutical compound in the presence of the gallic acid ester greater than the bioavailability of the pharmaceutical compound in the absence of the gallic acid ester when the pharmaceutical composition is administered orally to a mammal, wherein said gallic acid ester is selected from the group consisting of (-)-epicatechin gallate, (-)-epigallocatechin gallate and (-)-gallocatechin gallate.

59. A method of reformulating an existing oral pharmaceutical composition, the method comprising:

admixing the active compound of the existing oral pharmaceutical composition with a gallic acid ester, the gallic acid ester being present in sufficient amount to provide bioavailability of the active compound when administered in the reformulated composition greater than said bioavailability of the active compound when administered in the existing

pharmaceutical composition, wherein said gallic acid ester is selected from the group consisting of (-)-epicatechin gallate, (-)-epigallocatechin gallate and (-)-gallocatechin gallate.